

I. REMARKS

Claims 1-5 are pending. Claim 3 is withdrawn as being directed to non-elected subject matter. No amendments to the specification or claims are made at this time.

Claims 1 (in part), 2, 4, and 5-6 (in part) are rejected under 35 U.S.C. § 103(a) as being obvious over Del Soldato et al. (WO 95/30641) in view of Ara et al. ("Cyclooxygenase and lipxygenase inhibitors in cancer therapy, " Prostaglandins, Leukotrienes and Essential Fatty Acids 54: 3-16 (1996)). This rejection is traversed.

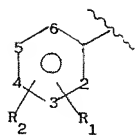
Applicants submit that this rejection was rendered moot, at least in part, by the previous cancellation of claim 6 in the response filed September 21, 2007.

Further to the previously filed remarks, Applicants respectfully submit that the evidence of unexpected results in the previously filed Declaration under 35 U.S.C. § 1.132 (filed October 10, 2003 and again on September 21, 2007 for the Examiner's convenience) is sufficient to overcome the *prima facie* case of obviousness asserted in the final Office Action. The Declaration shows the activity of the nitroxymethyl phenyl esters of aspirin (NO-Asp-1/2/3) and of flurbiprofen (4-nitrooxy)butyl ester (NO-flurbiprofen) in inhibiting precancerous cell formation and cancer cell growth in comparison to the reference non-nitroderivative compounds aspirin and flurbiprofen.

Applicants note that NO-Asp-1/2/3 are compounds of present claim 5. Further, Del Soldato et al. discloses NO-Asp-1/2/3 where, in the formula A-X₁-NO₂,

A= R(COX_u)_t wherein:

R is formula Ia) of group I)

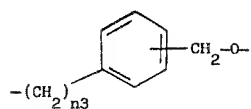


, wherein R_1 is $-\text{OCOCH}_3$ and R_2 is H,

X is $-\text{O}-$,

u and t are 1, and

X_1 is



, wherein n_3 is 0.

Meanwhile, the reference compounds (i.e., aspirin and flurbiprofen) compared in the Declaration with the compounds of the presently claimed invention are compounds disclosed in Ara et al. See, for example, page 6, left column, second full paragraph of Ara et al. disclosing “aspirin,” and page 9, left column, first full paragraph of Ara et al. disclosing “flurbiprofen.” As such, the Declaration clearly compares compounds of the presently claimed invention (and Del Soldato et al.) with compounds of Ara et al., the closest cited reference, in treating colon tumors.

Table 1 of the Declaration discloses that NO-Asp-1 is more effective than aspirin in preventing colon neoplastic lesion in an experimental model of colon adenocarcinoma. In fact, the precancerous cell number is reduced with the compound of the presently claimed invention (NO-Asp-1). Table 2 of the Declaration shows that NO-Asp-1/2/3 are much more effective in inhibiting the proliferation of the cancerous cells in vitro with respect to aspirin. Meanwhile, Table 3 of the Declaration shows that NO-flurbiprofen reduced the number of HT-29 cells (human colon adenocarcinoma cell line) in the culture

more effectively than flurbiprofen. As such, the Declaration shows the unexpected results of compounds of the presently claimed invention as compared with the compounds of Ara et al., the closest cited reference.

Accordingly, for at least the above reasons, applicants respectfully request reconsideration and withdrawal of the rejection of claims 1 (in part), 2, 4, and 5-6 (in part) under 35 U.S.C. § 103(a) as being obvious over Del Soldato et al. in view of Ara et al.

II. CONCLUSION

Applicants respectfully submit that this application is in condition for allowance and such action is earnestly solicited. If the Examiner believes that anything further is desirable in order to place this application in even better condition for allowance, the Examiner is invited to contact Applicants' undersigned representative at the telephone number listed below to schedule a personal or telephone interview to discuss any remaining issues.

In the event this paper is not considered to be timely filed, Applicant hereby petitions for an appropriate extension of time. The fee for this extension may be charged to our Deposit Account No. 01-2300, referring to Attorney Docket No. 026220-00039. Please charge any fee deficiency or credit any overpayment to Deposit Account No. 01-2300, referencing Attorney Docket No. 026220-00039.

Respectfully submitted,



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